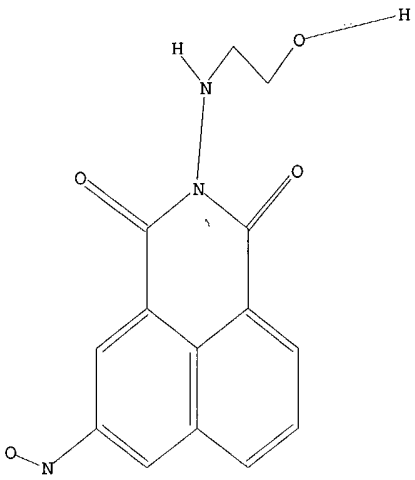
09758917

L2 STRUCTURE UPLOADED

=> d
L2 HAS NO ANSWERS
L2 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l2
SAMPLE SEARCH INITIATED 11:36:09 FILE 'BEILSTEIN'
SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 0 TO 0
PROJECTED ANSWERS: 0 TO 0

L3 0 SEA SSS SAM L2

=> s l2 sss full
FULL SEARCH INITIATED 11:36:19 FILE 'BEILSTEIN'
FULL SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.03

L4 0 SEA SSS FUL L2

=>

09758917

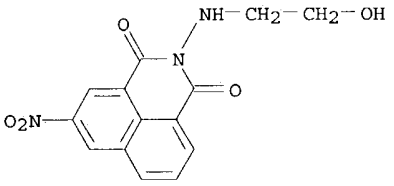
```
=> s e3
L1            1 234779-34-1/RN

=> d all

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   234779-34-1  REGISTRY
ED   Entered STN:  25 Aug 1999
CN   1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[(2-hydroxyethyl)amino]-5-nitro-
     (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   ALE 0540
FS   3D CONCORD
MF   C14 H11 N3 O5
SR   CA
LC   STN Files:   BIOSIS, CA, CAPLUS, CHEMCATS
```

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C5N-C6-C6	NC5-C6-C6	6-6-6	C12N	1784.14.8	1



Calculated Properties (CALC)

PROPERTY (CODE)	VALUE	CONDITION	NOTE
Bioconc. Factor (BCF)	1	pH 1	(1) ACD
Bioconc. Factor (BCF)	1	pH 4	(1) ACD
Bioconc. Factor (BCF)	1	pH 7	(1) ACD
Bioconc. Factor (BCF)	1	pH 8	(1) ACD
Bioconc. Factor (BCF)	1	pH 10	(1) ACD
Boiling Point (BP)	553.0+/-60.0 deg C	760.0 Torr	(1) ACD
Enthalpy of Vap. (HVAP)	87.73+/-3.0 kJ/mol		(1) ACD
Flash Point (FP)	288.3+/-59.2 deg C		(1) ACD
H acceptors (HAC)	8		(1) ACD
H donors (HD)	2		(1) ACD
Koc (KOC)	34.2	pH 1	(1) ACD
Koc (KOC)	34.2	pH 4	(1) ACD
Koc (KOC)	34.2	pH 7	(1) ACD
Koc (KOC)	34.2	pH 8	(1) ACD
Koc (KOC)	34.2	pH 10	(1) ACD
logD (LOGD)	0.29	pH 1	(1) ACD
logD (LOGD)	0.29	pH 4	(1) ACD
logD (LOGD)	0.29	pH 7	(1) ACD
logD (LOGD)	0.29	pH 8	(1) ACD
logD (LOGD)	0.29	pH 10	(1) ACD
logP (LOGP)	0.290+/-0.626		(1) ACD
Molar Solubility (SLB.MOL)	>=0.01 - <0.1 mol/L	pH 1	(1) ACD
Molar Solubility (SLB.MOL)	>=0.01 - <0.1 mol/L	pH 4	(1) ACD
Molar Solubility (SLB.MOL)	>=0.01 - <0.1 mol/L	pH 7	(1) ACD
Molar Solubility (SLB.MOL)	>=0.01 - <0.1 mol/L	pH 8	(1) ACD
Molar Solubility (SLB.MOL)	>=0.01 - <0.1 mol/L	pH 10	(1) ACD
Molecular Weight (MW)	301.25		(1) ACD
Vapor Pressure (VP)	4.59E-13 Torr	25.0 deg C	(1) ACD

(1) Calculated using Advanced Chemistry Development (ACD/Labs) Software
Solaris V4.67 ((C) 1994-2004 ACD/Labs)

09758917

See HELP PROPERTIES for information about property data sources in REGISTRY.
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

AN 135:298810 CA
TI Use of NGF antagonists for the prevention or treatment of chronic visceral pain
IN Diop, Laurent; Delafoy, Laure
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
ICS A61K031-473; A61K039-395; A61P015-00; A61P001-06; A61P001-18; A61P001-14; A61P001-00
CC 1-11 (Pharmacology)
Section cross-reference(s): 2, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001078698	A2	20011025	WO 2001-EP3490	20010326
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2807660	A1	20011019	FR 2000-4782	20000413
EP 1282421	A2	20030212	EP 2001-927818	20010326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001010028	A	20030603	BR 2001-10028	20010326
JP 2003530427	T2	20031014	JP 2001-575999	20010326
PRAI FR 2000-4782	20000413			
WO 2001-EP3490	20010326			

AB A nerve growth factor (NGF) antagonist is used for the manufacture of a medicament intended for the prevention or treatment of chronic visceral pain. Corresponding pharmaceutical compns. are also disclosed.
ST NGF antagonist chronic visceral pain treatment
IT Analgesics
Drug delivery systems
Dysmenorrhea
Dyspepsia
(NGF antagonists for prevention or treatment of chronic visceral pain)
IT Nerve growth factor receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NGF antagonists for prevention or treatment of chronic visceral pain)
IT Pain
(chronic; NGF antagonists for prevention or treatment of chronic visceral pain)
IT Digestive tract
(gastroesophageal reflux; NGF antagonists for prevention or treatment of chronic visceral pain)
IT Intestine, disease
(irritable bowel syndrome; NGF antagonists for prevention or treatment of chronic visceral pain)
IT Drug delivery systems
(oral; NGF antagonists for prevention or treatment of chronic visceral pain)
IT Viscera
(pain; NGF antagonists for prevention or treatment of chronic visceral pain)
IT Pancreas, disease
(pancreatitis; NGF antagonists for prevention or treatment of chronic visceral pain)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to NGF; NGF antagonists for prevention or treatment of chronic

visceral pain)
IT Viscera
(visceralgia; NGF antagonists for prevention or treatment of chronic visceral pain)
IT 234779-34-1, ALE 0540
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NGF antagonists for prevention or treatment of chronic visceral pain)
IT 137010-36-7, NGF receptor tyrosine kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NGF antagonists for prevention or treatment of chronic visceral pain)
IT 9061-61-4, Nerve growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NGF antagonists for prevention or treatment of chronic visceral pain)

REFERENCE 2

AN 131:125331 CA
TI Characterization of antiallodynic actions of ALE-0540, a novel nerve growth factor receptor antagonist, in the rat
AU Owolabi, Joshua B.; Rizkalla, Geihan; Tehim, Ashok; Ross, Gregory M.; Riopelle, Richard J.; Kamboj, Rajender; Ossipov, Michael; Bian, Di; Wegert, Sandara; Porreca, Frank; Lee, David K. H.
CS Allelix Biopharmaceuticals Inc., Mississauga, Can.
SO Journal of Pharmacology and Experimental Therapeutics (1999), 289(3), 1271-1276
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
CC 1-11 (Pharmacology)
AB There is growing evidence that nerve growth factor (NGF) may function as a mediator of persistent pain states. We have identified a novel nonpeptidic mol., ALE-0540, that inhibits the binding of NGF to tyrosine kinase (Trk) A or both p75 and TrkA (IC50 5.88±1.87 μM, 3.72±1.3 μM, resp.), as well as signal transduction and biol. responses mediated by TrkA receptors. ALE-0540 was tested in models of neuropathic pain and thermally-induced inflammatory pain, using two routes of administration, a systemic i.p. and a spinal intrathecal (i.t.) route. Morphine was also tested for comparison in the antiallodynia model using mech. stimuli. We show that either i.p. or i.t. administration of ALE-0540 in rats produced antiallodynia in the L5/L6 ligation model of neuropathic pain. The calculated A50 values (and 95% confidence intervals) for ALE-0540 administered i.p. and i.t. were 38 (17.5-83) mg/kg and 34.6 (17.3-69.4) μg, resp. ALE-0540 given i.t., at doses of 30 and 60 μg, also blocked tactile allodynia in the thermal sensitization model. Although morphine displayed greater potency [A50 value of 7.1 (5.6-8.8) mg/kg] than ALE-0540 in anti-allodynic effect when given i.p. to L5/L6-ligated rats, it was not active when administered i.t. These data suggest that a blockade of NGF bioactivity using a NGF receptor antagonist is capable of blocking neuropathic and inflammatory pain and further support the hypothesis that NGF is involved in signaling pathways associated with these pain states. ALE-0540 represents a nonpeptidic small mol. which can be used to examine mechanisms leading to the development of agents for the treatment of pain.
ST ALE 0540 antiallodynia nerve growth factor
IT Pain
Skin, disease
(allodynia; characterization of antiallodynic actions of ALE-0540, a novel nerve growth factor receptor antagonist, in the rat)
IT Analgesics
(characterization of antiallodynic actions of ALE-0540, a novel nerve growth factor receptor antagonist, in the rat)
IT Nerve growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(characterization of antiallodynic actions of ALE-0540, a novel nerve growth factor receptor antagonist, in the rat)
IT 234779-34-1, ALE 0540
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of antiallodynic actions of ALE-0540, a novel nerve growth factor receptor antagonist, in the rat)
IT 9061-61-4, Nerve growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(characterization of antiallodynic actions of ALE-0540, a novel nerve growth factor receptor antagonist, in the rat)

09758917

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD

(1) Aloe, L; Arthritis Rheumat 1992, V35, P351 MEDLINE
(2) Andreev, N; Pain 1995, V63, P109 CAPLUS
(3) Averill, S; Eur J Neurosci 1995, V7, P1484 MEDLINE
(4) Chaplan, S; J Neurosci Methods 1994, V53, P55 MEDLINE
(5) Chung, K; Neurosci Lett 1993, V162, P85 MEDLINE
(6) Crowley, C; Cell 1994, V76, P1001 CAPLUS
(7) Diamond, J; Proc Natl Acad Sci USA 1987, V84, P6596 CAPLUS
(8) Dixon, W; Annu Rev Pharmacol Toxicol 1980, V20, P441 MEDLINE
(9) Donnerer, J; Neuroscience 1992, V49, P693 CAPLUS
(10) Dostaler, S; Eur J Neurosci 1996, V8, P870 MEDLINE
(11) Greene, L; Proc Natl Acad Sci USA 1976, V73, P2424 CAPLUS
(12) Heumann, R; J Cell Biol 1987, V104, P1623 CAPLUS
(13) Jaen, J; J Med Chem 1995, V38, P4439 CAPLUS
(14) Kaplan, D; Nature (Lond) 1991, V350, P158 CAPLUS
(15) Karlsten, R; Neurosci Lett 1991, V121, P267 CAPLUS
(16) Kim, S; Pain 1992, V50, P355 MEDLINE
(17) Lewin, G; Eur J Neurosci 1994, V6, P1903 MEDLINE
(18) Lewin, G; J Neurosci 1993, V13, P2136 CAPLUS
(19) Lewin, G; Trends Neurosci 1993, V16, P353 CAPLUS
(20) Max, M; Clin Pharmacol Ther 1988, V43, P363 MEDLINE
(21) May, A; Pain 1996, V67, P375 CAPLUS
(22) Mazzari, S; Eur J Pharmacol 1996, V300, P227 CAPLUS
(23) McMahon, S; Nat Med 1995, V1, P774 CAPLUS
(24) Murphy, R; J Neurosci 1993, V13, P2853 CAPLUS
(25) Nichols, M; Soc Neurosci Abstr 1995, V21, P1172
(26) Pertovaara, A; Eur J Pharmacol 1990, V179, P323 CAPLUS
(27) Petty, B; Ann Neurol 1994, V36, P244 CAPLUS
(28) Porreca, F; Life Sci 1983, V33, P457 CAPLUS
(29) Ramer, M; Pain 1997, V70, P237 MEDLINE
(30) Ramer, M; Soc Neurosci Abstr 1995, V21, P897
(31) Ritter, A; Nature (Lond) 1991, V350, P500 CAPLUS
(32) Ross, G; Eur J Neurosci 1998, V10, P890 MEDLINE
(33) Spiegel, K; Biochem Biophys Res Commun 1995, V217, P488 CAPLUS
(34) Suh, H; Neuropeptides 1996, V30, P485 CAPLUS
(35) Sutter, A; J Biol Chem 1979, V254, P5972 CAPLUS
(36) Wiesenfeld-Hallin, Z; Regul Pept 1996, V65, P23 CAPLUS
(37) Woolf, C; Curr Opin Neurobiol 1994, V4, P525 MEDLINE
(38) Woolf, C; Neuroscience 1994, V62, P327 CAPLUS
(39) Xu, X; Pain 1991, V46, P223 CAPLUS
(40) Yaksh, T; Physiol Behav 1976, V17, P1031 MEDLINE